Direct 3D bioprinting of prevascularized tissue constructs with complex microarchitecture.

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Public Summary:
In this work, we present a rapid DLP based bioprinting method - microscale continuous optical bioprinting (μCOB) - to create prevascularized tissue constructs directly with unprecedented speed and resolution. The 3D-printed prevascularized tissues have complex microarchitecture and precisely controlled distribution of multiple cell types and biomaterial compositions. To simplify and speed up the tissue engineering process, endothelial cells and mesenchymal cells were printed directly into the designed vascular channels without the use of sacrificial material or perfusion. These cells formed lumen-like structures and functional endothelial networks spontaneously both in vitro and in vivo, which provides a much simpler and more efficient platform for engineering tissues with complex structures and functions. This computer-aided photopolymerization-based 3D bioprinting system offers superior speed, resolution, flexibility and scalability over the conventional bioprinters. Its digital nature also provides the flexibility to easily investigate different designs, which is a key to studying the architectural features of the vasculature network. The prevascularized tissues printed by μCOB demonstrated high cell viability and successful endothelial network formation both in vitro and in vivo. Anastomosis between the grafted prevascularized tissues and the host vasculature was observed indicating the formation of functional vasculature in engineered tissues. This platform can be further extended to engineer other tissues that feature complex microarchitectures, such as liver, heart and nerve tissues. By incorporating the prevascularization technique with other primary or stem cells we can potentially engineer functional large-scale tissues for drug testing or even organs for transplantations. With the high resolution and rapid printing speed, it's relatively easy to scale up to print large hollow vessels for blood flow. Future work can be done to print large vessels and micro-vasculature network together for large tissue constructs. Also, the large scale tissue can be integrated into fluidic devices/bioreactors to simulate blood flow and promote diffusion. With its versatility and biocompatibility, the presented engineering strategy of building vascularized 3D tissues can be broadly applied to promote the development and translation of tissue engineering and regenerative medicine.

Scientific Abstract:
Living tissues rely heavily on vascular networks to transport nutrients, oxygen and metabolic waste. However, there still remains a need for a simple and efficient approach to engineer vascularized tissues. Here, we created prevascularized tissues with complex three-dimensional (3D) microarchitectures using a rapid bioprinting method - microscale continuous optical bioprinting (muCOB). Multiple cell types mimicking the native vascular cell composition were encapsulated directly into hydrogels with precisely controlled distribution without the need of sacrificial materials or perfusion. With regionally controlled biomaterial properties the endothelial cells formed lumen-like structures spontaneously in vitro. In vivo implantation demonstrated the survival and progressive formation of the endothelial network in the prevascularized tissue. Anastomosis between the bioprinted endothelial network and host circulation was observed with functional blood vessels featuring red blood cells. With the superior bioprinting speed, flexibility and scalability, this new prevascularization approach can be broadly applicable to the engineering and translation of various functional tissues.